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# The Cough Suppressant Effect of Heroin and Codeine: A Controlled Clinical Study

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A RECENT assessment of two new cough suppressants showed them to be of little value in decreasing the cough of chronic bronchitis.[1, 2] It was subsequently decided to study two long-established and widely accepted cough preparations, namely elixir of terpin hydrate with heroin, and syrup of codeine. We have found no reports of a double-blind controlled clinical study of either preparation in the English medical literature.

In the controlled investigation described in this report it will be shown that, in patients with chronic cough, the addition of heroin to elixir of terpin hydrate adds nothing to the cough suppressant effect of the elixir alone. Codeine when added to a syrup does have a small but significantly better cough suppressant action than the syrup alone.

## MATERIAL AND METHODS

All the subjects were male inpatients of Sunnybrook Hospital who had chronic cough. The patients were considered to be in a stable state as far as their chest disease was concerned, and no cough medications other than the test mixtures were administered during the trial.

### *A study of elixir of terpin hydrate with heroin*

Fourteen patients, ranging in age from 39 to 74 years with a mean age of 62 years, took part in this investigation. Four patients had chronic bronchitis, six had bronchitis with emphysema, three had carcinoma of the lung and one had diffuse pulmonary fibrosis.

Bottles of elixir of terpin hydrate with heroin (1/24 grain in 60 minims) and elixir of terpin hydrate without heroin were made up in pairs by the hospital pharmacist. The addition of heroin to elixir of terpin hydrate (ETH) did not alter the appearance or taste of the mixture. The trial was of a double-blind type. The patient was given 60 minims of the mixture with a little water added, at 5:00 p.m., and this was repeated at 9:00 p.m., at 8:00 a.m. next morning, at 12 noon, and at 4:00 p.m. He therefore received five doses over 24 hours. During this period his sputum was collected and measured. At the end of the 24 hours the following questionnaire was filled in by direct questioning:

Has your cough changed since taking the treatment? Yes/No

If yes, is it worse? Yes/No
less? Yes/No
If less, has it decreased: Slightly?
Considerably?
When did the change occur?

If the patient claimed that the cough was unchanged or worse, the mixture in the second of the paired bottles was given in the same way as before, the sputum was measured and a questionnaire was completed. If the patient claimed a decrease in cough after the first mixture, no further treatment was given until the cough returned to its previous intensity. Then the second mixture was given. The bottles were arranged so that some patients received first ETH and then ETH with heroin, and for others the order was reversed. The forced expiratory volume (one second) and the forced vital capacity were measured, using a Gaensler-Collins timed vitalometer, immediately prior to starting treatment and after each 24-hour period of treatment.

After the second period of treatment the patient was asked which medicine he preferred.

### *A study of syrup of codeine*

Thirty patients took part in this investigation, ranging in age from 37 to 80 years, with a mean age of 58 years. Eighteen patients had bronchitis with emphysema, seven had chronic bronchitis, four had carcinoma of the lung, and one had pulmonary fibrosis.

Syrup of codeine consists of simple syrup, spirits of chloroform codeine (1/4 grain in each 60 minims). A mixture of identical colour and taste was prepared by adding Love's egg-yolk colour, tincture of gentian compound and spirits of chloroform to simple syrup. Bottles of syrup of codeine and the simple syrup were made up in pairs, and the investigation followed almost the same lines as the heroin study. The only difference was that the patient was given 120 minims of the mixture containing codeine 1/2 grain at 6:00 p.m., 10:00 p.m., 6:00 a.m., 10:00 a.m. and 2:00 p.m., these times being in accord with the usual medication rounds. The medicine was undiluted and was sipped. Ventilation tests were not performed.

## RESULTS

The effect on cough of elixir of terpin hydrate alone and of elixir of terpin hydrate with heroin is shown in Table I. Ten of the 14 patients claimed a decrease in cough after ETH alone, and 11 claimed improvement after ETH with heroin.

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TABLE I.—EFFECT ON COUGH AND VENTILATION OF ELIXIR OF TERPIN HYDRATE (ETH) ALONE AND OF ELIXIR OF TERPIN HYDRATE WITH HEROIN

| | | *ETH* | *ETH with heroin* |
|---|---|---|---|
| Cough | No change | 4 | 2 |
| | Slight decrease | 3 | 9 |
| | Considerable decrease | 7 | 2 |
| | Increase | 0 | 1 |
| F.E.V.$_1$ | No change | 13 | 12 |
| | Decrease | 0 | 0 |
| | Increase | 1 | 1 |
| F.V.C. | No change | 13 | 12 |
| | Decrease | 0 | 0 |
| | Increase | 1 | 1 |

Ventilation studies were omitted in one of the patients after taking ETH with heroin.

Seven patients reported a considerable decrease in the cough after ETH, and two reported a considerable decrease from ETH with heroin. The results of sputum volume measurements are shown in Table II. A sputum volume change greater than half an ounce was arbitrarily considered significant. Sputum volumes remained remarkably constant irrespective of the type of treatment. Only four patients showed a decreased sputum volume, all after the 24 hours of treatment with ETH and heroin. There was no significant change in ventilation after use of either of the mixtures. When asked which medicine they preferred, five patients had no preference, six patients preferred ETH alone and three preferred ETH with heroin. The investigation using these 14 patients was originally intended as a pilot study, but the results were so unequivocal that it was decided not to extend the investigation.

The effect on cough of syrup of codeine compared with the simple syrup is shown in Table III. Twelve of the 30 patients claimed a decrease in cough after simple syrup, and 20 claimed improvement after syrup of codeine. Statistical analysis by the chi square test showed this difference to be just significant ($p < 0.02$). Four patients reported considerable decrease in cough after the simple syrup, and nine claimed considerable improvement after syrup of codeine. This difference is not statistically significant ($p < 0.05$). The results of the sputum volume measurements are shown in Table II. Seven patients showed a decrease in sputum volume after syrup of codeine, and three patients had a decrease in sputum volume after the simple syrup. When asked which medicine they preferred, 10 patients said that they had no preference, six preferred the simple syrup and 14 preferred syrup of codeine.

TABLE II.—SPUTUM VOLUME RESULTS

| | |
|---|---|
| ETH with heroin compared with ETH: | |
| No change | 9 |
| Decrease | 4 |
| Increase | 0 |
| No collection | 1 |
| Syrup of codeine compound with simple syrup: | |
| No change | 16 |
| Decrease | 7 |
| Increase | 3 |
| No collection | 4 |

TABLE III.—EFFECT ON COUGH OF SIMPLE SYRUP AND OF SYRUP OF CODEINE

| | | *Simple syrup* | *Syrup of codeine* |
|---|---|---|---|
| Cough | No change | 17 | 10 |
| | Slight decrease | 8 | 11 |
| | Considerable decrease | 4 | 9 |
| | Increase | 1 | 0 |

## DISCUSSION

Regret has been expressed by many physicians that such an excellent cough suppressant as elixir of terpin hydrate with heroin is no longer generally available in Canada. In the present investigation, patients were unable to distinguish between ETH with and without heroin. This is not surprising when one considers that the amount of heroin in each dose is only 1/24 grain and that this is given by mouth. The schedule of five doses of the heroin mixture in 24 hours might be considered sufficient by most physicians. It is of interest that elixir of terpin hydrate itself consists of the following: terpin hydrate 8 grains, saccharine ¼ grain, extract vanilla 12½ minims, fluid extract of liquorice 4½ minims, fluid extract of cascara 9 minims, ethyl alcohol 38⅛%, glycerin 38⅛%, caramel for colouring, water added to 1 oz. Terpin hydrate is prepared by the action of nitric acid on turpentine oil in the presence of alcohol, the resulting crystals being filtered off or crystallized from alcohol.[3] The present investigation suggests that the beneficial effect of ETH with heroin lies in the elixir of terpin hydrate which itself is a complex mixture.

There is no evidence that any one physician was responsible for the introduction of cough syrup. Boyd[4] states that the beneficial effect of sugar or syrup held in the mouth was probably discovered by the common people by trial and error. A simple syrup has relieved cough due to colds in 68% of 28 patients.[4] In the present investigation, although many patients did obtain relief of cough from the simple syrup, a small but significantly better effect was obtained by the addition of codeine.

The patients included in the present study were mostly in the older age groups and all had chronic cough. The conclusions made are applied only to this type of patient and might not be relevant in the case of coughs of a more transient or acute nature. The evidence presented suggests that elixir of terpin hydrate is useful for the relief of cough. When the use of syrup of codeine is considered, one should weigh the disadvantages of codeine against its only slight advantage over a simple syrup as a cough suppressant.

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SUMMARY

Using a double blind technique, it has been shown in 14 patients with chronic cough that the cough suppressant effect of elixir of terpin hydrate alone was similar to that of elixir of terpin hydrate with heroin.

In a comparison between a simple syrup and syrup of codeine, 12 of 30 patients claimed some improvement in cough from the simple syrup, and 20 of the 30 patients reported improvement after the syrup of codeine. This indicated a small but statistically significantly better effect from the syrup of codeine.

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# Urinary Tuberculosis: A Review of 50 Cases

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IN RECENT years the incidence of urinary tuberculosis has markedly decreased. However, in Newfoundland, where all forms of tuberculosis still constitute a major problem, the authors have had an opportunity to study 50 cases of urinary tuberculosis in patients admitted to sanatoria in the period from 1958 to 1961 inclusive.

The morbidity and mortality from tuberculosis in Newfoundland have been the highest in Canada, but remarkable changes have occurred in the past decade with the advent of chemotherapy and improved surgical techniques. In this area, other factors contributing towards the decreased morbidity have been a much-improved case-finding program, use of B.C.G. vaccine, and a general improvement in economic conditions.

TABLE I.—COMPARISON OF TUBERCULOSIS MORBIDITY AND NUMBER OF DEATHS FROM TUBERCULOSIS IN 1950 AND 1960

| | | *Nfld.* | *Canada* |
|---|---|---|---|
| Morbidity (per 100,000 population) | 1950 | 70.4 | 26.8 |
| | 1960 | 8.9 | 4.6 |
| Number of deaths | 1950 | 247 | 3679 |
| | 1960 | 41 | 823 |

Urinary tuberculosis is secondary to disease elsewhere in the body, frequently to a pulmonary lesion. Hematogenous dissemination occurs, and the disease becomes manifest in the urinary tract.[1]

The purpose of this paper is to report the details of the diagnosis and management of 50 cases of urinary tuberculosis. In this series there was a marked male preponderance: 66% were males and 34% females.

The highest incidence of urinary tuberculosis was in the 30-40 year age group, followed by the 40-50 year age group. This is similar to findings in other series.[2-5] Only 24% of the patients were under 30 years of age.

TABLE II.—AGE INCIDENCE

| *Age group* | *Number of patients* | *% of patients* |
|---|---|---|
| 10 - 19 | 5 | 10 |
| 20 - 29 | 7 | 14 |
| 30 - 39 | 19 | 38 |
| 40 - 49 | 11 | 22 |
| 50 - 59 | 8 | 16 |
| Total | 50 | 100 |

## EXTENT OF DISEASE

Lattimer's classification is used to define the extent of disease as follows: "Minimal disease" refers to bacilluria without visible radiological changes. "Moderately advanced" indicates disease confined to one major calyx. "Far advanced" refers to tuberculous lesions extending beyond the confines of one major calyx.

In our series, 72% of the cases were far advanced and presented greater problems in management.

TABLE III.—EXTENT OF DISEASE

| | *Number of patients* | *% of patients* |
|---|---|---|
| Minimal | 6 | 12 |
| Moderately advanced | 8 | 16 |
| Far advanced | 36 | 72 |
| Total | 50 | 100 |

### *Other Foci*

In the great majority of cases of urinary tuberculosis there are other associated tuberculous lesions. In our series, 82% of the patients had other demonstrable foci, of which pulmonary lesions were by far the most common.

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